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| EXAMINER | |
|---|---|
| SWOPE, SHERIDAN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1652 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/526,768 | KLUSSMANN ET AL. | |
| | Examiner | Art Unit | |
| | SHERIDAN SWOPE | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *6-8 and 11-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9,10 and 20* is/are rejected.

7)☒ Claim(s) *18 and 19* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1208*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicants' Request for Continuing Examination filed December 30, 2008, in response to the Action mailed July 30, 2008, is acknowledged. It is acknowledged that applicants have amended Claims 1, 2, 19, and 20. Claims 1-20 are pending. Claims 6-8 and 11-17 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1-5, 9, 10, and 18-20 are hereby reconsidered.

It is noted that the Examiner contacted Applicants' representative, Anthony Zelano, on February 3 and 5, 2009 to discuss a possible Examiner's Amendment. On about February 19, 2008, Mr Zelano requested an Interview with the Examiner, which was agreed upon for March 5, 2009. On March 5, 2009, Mr Zelano, did not contact the Examiner and, upon calling his office, the Examiner was informed that Mr Zelano was out of the office for the day. The Examiner spoke with Mr Zelano's assistant, Sagun KC; no agreement as to amendment of the claims was reached.

### *Sequence Listing*

Objection to the sequence listing because it continues to annotate SEQ ID NO: 1 as a human protein, while GenEMBL annotates SEQ ID NO: 1 as a rat protein (Accession no. AY350741/GI:37993505), is maintained.

***Claim Rejections - 35 USC § 112-Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejection of Claims 4, 5, 9, and 10 under 35 U.S.C. 112, second paragraph, as being indefinite because the phrase "a nucleic acid molecule according to Claim 1" in Claims 4, 9, and 10, should be amended to "the nucleic acid molecule according to Claim 1", is maintained.

***Claim Rejections - 35 USC § 112-First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Enablement**

Rejection of Claims 1, 3-5, 9, 10, and 20 under 35 U.S.C. 112, first paragraph/enablement, for essentially the same reasons explained in the prior actions, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(A) Applicants traverse the PTO's contention that the specification must provide explicit guidance as to which domains, motifs, or amino acid residues may be altered in the claimed variant polynucleotide[s]. The art is replete with information on degeneracy of the genetic code, conserved amino acid substitutions, replacement of analogous amino acid residues with structurally similar amino acids, and the like. Examples of such conserved substitutions are herein provided. One skilled in biochemistry also knows that variant polynucleotide sequences are not limited to degenerate codes or conserved amino acid substitutions, as enantiomeric

substitutions and amino acid modifications in accordance with WO 99/62933 or WO 02/38592 are also possible. The publications enclosed herewith explicitly teach that it is possible to replace single amino acids or groups of amino acids in a polypeptide chain without adversely affecting the activity of the resulting peptides.

(B) Polypeptides that are encoded by the encompassed variant polynucleotides can be analyzed with respect to primary and secondary structure(s). Other in vitro assay techniques comprising the use of recombinant proteins, for example, binding assays, enzymatic assays, activity assays and the like, may similarly be employed. The whole process constitutes nothing more than what is routine in the art. See Schneideret al (PNAS, 1998) and Hundrucker (Biochem J., 2006; Table 2).

These arguments are not found to be persuasive for the following reasons.

(A) Reply: It is acknowledged that the degeneracy of the genetic code is known.

Although very common in the art, the term "conservative substitution" is vague and indefinite. For example, is a Gln/Glu substitution or an Asp/Asn substitution conservative? Are Ser/Tyr and Phe/Tyr conservative substitutions? Another situation that is indefinate is the classification of Gly and Ala; are these small polar residues, similar to Ser, Thr, Gln and Asn, or hydrophobic? Is His basic or hydrophobic? Are linear hydrophobic amino acids similar to aromatic hydrophobic amino acids? Is Cys a small polar amino acid or its own category? Is Tyr a polar amino acid or an aromatic amino acid? Lack of consensus on the answers to these questions causes the term "conservative substitution" to be indefinite.

It is acknowledged that Applicants' response has provided a list of examples of conserved substitutions; however the specification fails to disclose said list of examples. The specification also fails to disclose the teachings of WO 99/62933 or WO 02/38592.

As explained in the prior actions, methods for making variant polynucleotides were known in the art. Claims 1, 3-5, 9, and 10 encompass a very large genus of polynucleotides, wherein the polynucleotides encode polypeptides with any or no activity. The specification fails to enable the skilled artisan make and use all species of said very large genus of polynucleotides. Claim 20 encompasses a very large genus of polynucleotides wherein the polynucleotides encode polypeptides with protein kinase A regulator subunit II binding activity. As explained in the prior action, said genus encompasses polynucleotides encoding $3 \times 10^{23}$ variants of the polypeptide set forth by SEQ ID NO: 2. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification. Thus, without the needed explicit guidance as to which domains, motifs, or amino acid residues may, or may not, be altered in the claimed variant polynucleotides, the public is reduced to trial and error making and testing all encoded variant polypeptides for binding to any protein having any structure and having protein kinase A regulator subunit II activity. Clearly said making and testing would be undue experimentation.

(B) None of Claims 1, 3-5, 9, and 10 recites a functional limitation of binding activity or enzymatic activity for the encoded polypeptides. It is acknowledged that Claim 20 recites the functional limitation of binding activity for any protein having any structure and having protein

kinase A regulator subunit II activity. As explained in the prior actions and (A), above, it would be undue experimentation to make 3 x $10^{23}$ variants of the polypeptide set forth by SEQ ID NO: 2 and test all said variant polypeptides for binding to any protein having any structure and having protein kinase A regulator subunit II activity.

Schneider et al, 1998 cannot provide enablement for the instant claims because it only discloses design of variant peptides of only 10 amino acids; Schneider et al does not teach making variant proteins. Hundrucker et al, 2006 cannot provide enablement for the instant claims because it was published after Applicants' priority date.

**Written Description**

Rejection of Claim 20 under 35 U.S.C. 112, first paragraph/written description, for essentially the same reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following argument.

(C) Claims 1-5, 9, 10, 18, 19, and 20, as amended, conform to exemplary claims 1 and 2 of Example 11B beginning on Page 39 of the Training Materials (Rev. 1, March 25, 2008) of the PTO's new Written Description Guidelines. The exemplary claims in said example are:

> Claim 1. An isolated nucleic acid that encodes a polypeptide with at least 85% amino acid sequence identity to SEQ ID NO: 2.
>
> Claim 2. An isolated nucleic acid that encodes a polypeptide with at least 85% amino acid sequence identity to SEQ ID NO: 2; wherein the polypeptide has activity Y.

The guidelines state that both of the above claims satisfy the requirement under 35 USC 112, first paragraph. With respect to claim 2, it is stated that "[although] the specification fails to teach which of the nucleic acid sequences that encode a polypeptide with at least 85% sequence identity to SEQ ID NO: 2 encode a polypeptide having the required activity Y .... the specification identifies domains responsible for activity Y." The guidelines further state that

"Although conservative amino acid substitutions in these domains will not necessarily result in a protein having activity Y, those of ordinary skill in the art would expect that many of these conservative substitutions would result in a protein having the required activity".

This conforms to Applicants' present invention wherein the claimed AKAP8 polynucleotide of SEQ ID NO: 1 encodes a protein of SEQ ID NO: 2 which has a novel activity (for example, AKAP8 protein anchors protein kinase A (PKA) with Ca2+ channels or receptors in cells, as recited in present claim 20).

This argument is not found to be persuasive for the following reasons.

(C) Reply: It is acknowledged that Claims 1-5, 9, 10, 18 and 19 conform to the Written Description requirement, as exemplified by the Guidelines Example 11B, Claim 1.

However, unlike Claim 2 in Example 11B, the instant specification fails to teach which domains, motifs, or amino acid residues of SEQ ID NO: 2 may or may not be altered and still retain the desired activity of binding to any protein having any structure and having protein kinase A regulator subunit II activity. Therefore, Claim 20 does not conform to Example 11B of the Training Materials of 2008 for the USPTO's new Written Description Guidelines.

For these reasons and those explained in the prior action, rejection of Claim 20 under 35 U.S.C. 112, first paragraph/written description is maintained.

***Allowable Subject Matter***

Claims 18 and 19 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated any new grounds of rejection presented in this Office action. Any new references were cited solely to support rejection based or amendment or rebut Applicants' arguments. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

**Final Comments**

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652